No. 2014-1209

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

CREAGRI, INC., a California Corporation,

Plaintiff-Appellant,

v.

PINNACLIFE, INC., a Nevada Corporation,

Defendant-Appellee.

APPEAL FROM THE UNITED STATES DISTRICT COURT FOR THE NORTHERN DISTRICT OF CALIFORNIA IN CASE NO. 11-CV-06635-LHK, JUDGE LUCY H. KOH

BRIEF FOR DEFENDANT-APPELLEE PINNACLIFE, INC.

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CERTIFICATE OF INTEREST

In compliance with Federal Circuit Rule 47.4, counsel for the Appellee Pinnaclife, Inc. certifies the following:

1. The full name of every party or *amicus* represented by the undersigned counsel in this case is Pinnaclife, Inc.

2. The name of the real party in interest is Pinnaclife, Inc.

3. Pinnaclife, Inc. does not have any parent corporation and no publicly held company owns 10 percent or more of its stock.

4. The names of all law firms and the partners or associates that appeared for Pinnaclife, Inc. in the trial court or are expected to appear for Pinnaclife, Inc. in this Court are:

BRYAN CAVE LLP

Kenneth Lee Marshall
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Nicholas A. Lind

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PRELIMINARY STATEMENT

Appellant CreAgri, Inc. ("CreAgri"), a California corporation allegedly selling olive-based nutritional supplements over the internet, brought this lawsuit against Pinnaclife, Inc. ("Pinnaclife") without even purchasing, much less testing, Pinnaclife's publicly-available accused products. CreAgri asserted two patents in this litigation: (1) U.S. Patent No. 6,416,808 (the "'808 Patent"), which includes claims expressly limited to certain ratios of olive-derived phenolic compounds; and (2) U.S. Patent No. 8,216,599 (the "'599 Patent"), which includes method claims of treating specific inflammatory conditions using a treatment agent containing the same olive-derived phenolic compounds.

As the district court correctly found, these patents are invalid for numerous reasons. The '808 Patent is anticipated by multiple references, all of which disclose olives naturally containing the claimed ratios of phenolic compounds. The '599 Patent is invalid under both 35 U.S.C. §§ 101 and 112 because CreAgri had no evidence in the patent or elsewhere that the claimed treatment agents had any effect on the claimed inflammatory conditions. CreAgri failed to create any material issue of disputed fact, and the judgment of invalidity should be upheld in its entirety.

STATEMENT OF FACTS

A. Accused Products

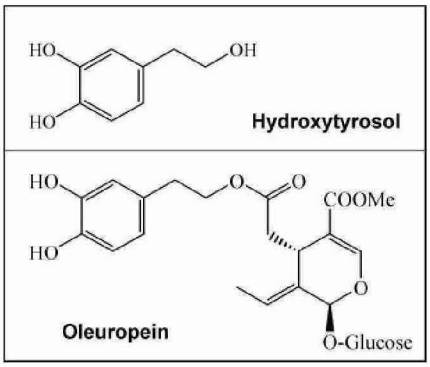
Pinnaclife's olivamine product line (the "Accused Products") consists of supplements containing antioxidants derived from olives, including the naturally-occurring polyphenolic compounds hydroxytyrosol, oleuropein, and tyrosol. (JA2125). Importantly, each of the Accused Products contains more oleuropein than hydroxytyrosol. (JA2126-27). With the exception of the Omega-3 product, the Accused Products are formulated in powder or powder-containing capsules. As to the Omega-3 supplement, all of the ingredients are powder with the exception of fish oil, which is added to incorporate omega-3 and is not an aqueous solution. (JA2126).

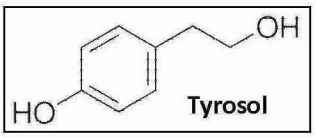
B. The Patents-In-Suit

Both asserted patents require incorporation of phenolic compounds—hydroxytyrosol, oleuropein, and tyrosol—derived from olives in specified weight ratios, into the claimed composition or method. (JA861,JA880). As described in the Background of the '808 Patent, it was widely known that olives contain compounds that, when ingested, provide beneficial health effects. These health effects were thought to be attributable to phenolic compounds—compounds containing a phenol ($-C_6H_5OH$) group—which are present in both olive oil and waste water obtained from industrial olive oil production, known as "vegetation

water." (JA874). In particular, the polyphenolic compounds oleuropein and hydroxytyrosol were thought to possess anti-oxidant and anti-inflammatory properties. (JA874(col.2,ln.9-30);JA945-949). Tyrosol, although also a phenol, did not appear to have the same desirable properties attributed to oleuropein and hydroxytyrosol. (JA875(col.4,ln.43-46)).

Long before the invention claimed in the '808 Patent, scientists understood that oleuropein was broken down into hydroxytyrosol through acid hydrolysis, either naturally within the olive or by exposure to acid and water in the laboratory. (JA874(col.2,ln.14-18),JA950,JA955). The structures of oleuropein and hydroxytyrosol illustrate that hydroxytyrosol is a hydrolysis product of oleuropein. Tyrosol is similar to hydroxytyrosol, but is missing one hydroxyl (-OH) group.





Under appropriate acidification conditions, oleuropein is converted into hydroxytyrosol along with other byproducts, while tyrosol remains intact. (JA875(col.4,ln.43-46)). The resulting composition consists of, over time, decreasing amounts of oleuropein, increasing amounts of hydroxytyrosol, and stable amounts of tyrosol. The acid hydrolysis reaction reaches an equilibrium

state, whereby no further hydroxytyrosol is produced and some oleuropein remains stable. (JA900-902).

1. The '808 Patent

The '808 Patent specification discloses methods for obtaining hydroxytyrosol-rich compositions from olive-derived vegetation water. (JA874(col.2,ln.33-39),JA875(col.4,ln.31-33)). Vegetation water is obtained by pressing olives to obtain a liquid-phase mixture including olive oil, vegetation water, and solid by-products, then separating the vegetation water from the rest of the liquid. (JA875). Olive pits, the primary source of the monophenolic compound tyrosol, may be removed prior to pressing. (JA874(col.2,ln.47-48),JA875(col.4,ln.40-41)). The resulting vegetation water contains an abundance of polyphenols, including oleuropein and its derivatives. (JA874(col.2,ln.41-49)).

The '808 Patent describes a method for increasing the hydroxytyrosol content of vegetation water through acid hydrolysis. (JA876(col.5,ln.25-31)). Notably, the '808 Patent does not contain any method claims. Rather, all claims of the '808 Patent are directed to compositions for use as dietary supplements. The two independent claims are directed to aqueous extracts of olives containing specific weight ratios requiring more hydroxtytyrosol than oleuropein and tyrosol:

> 1. A dietary supplement comprising an aqueous extract of olives containing a weight ratio of hydroxytyrosol to oleuropein of between about 5:1 and about 200:1.

> **5**. A dietary supplement comprising an aqueous extract of olives containing a weight ratio of hydroxytyrosol and tyrosol of between about 3:1 and about 50:1.

Dependent claims 2 and 6 narrow the ratios of claims 1 and 5. Claim 3 depends from claim 1 and contains the further limitation that the dietary supplement is dried to provide a powder extract. Claim 4 also depends from claim 1 and additionally requires the extract to be in the form of a tablet, capsule, pill, or confection food additive.

2. Key Prior Art

a. U.S. Patent No. 6,358,542 ("Cuomo")

Cuomo, which issued on March 19, 2002, from an application filed on December 20, 1999, discloses precisely the method of collecting olive waste water and acidification described in the '808 Patent. (JA1029). Indeed, the aqueous extract of olives and its resulting analysis is described repeatedly throughout Cuomo:

> As discussed above, one step of the conventional olive oil production process includes making a slurry of olive solids, olive oil, and water. The water and olive oil are pressed out of the slurry and separated, then the oil is separated from the water by decantation or centrifugation. This "water", referred to herein as "wastewater", is actually a solution of water-soluble antioxidant components, possibly along with small amounts of other materials left over from the olive oil manufacturing process. In this embodiment, this wastewater is used as the starting material in a method of preparing an antioxidant composition. Thus, it is a particular advantage of

(JA1041(col.9,ln.20-30)).

> The present invention provides methods of extracting anti-oxidant compositions from olive-based starting materials, including olives, olive pulps, olive oil, and wastewater from olive oil manufacturing. One method includes the steps of

(JA1029(Abstract)).

> In one embodiment, the present invention provides a method of preparing an antioxidant composition from an olive, an olive pulp, or an olive oil. The method includes the steps of extracting the starting material with a polar aqueous solvent to form an aqueous phase containing antioxidant components, passing the aqueous phase through a solid matrix to trap the antioxidant components on the matrix, and washing the matrix with a polar organic solvent to yield a solution of the antioxidant composition in the polar organic solvent.

(JA1039(col.5,ln.58-65)).

> In another step, the starting material is extracted with a polar aqueous solvent to form an aqueous phase containing antioxidant components extracted from the starting material. The extraction step can be carried out in any convenient fashion known to those skilled in the art. Preferably, when the starting material includes olives, the olives are pitted and crushed, chopped, ground, or subjected to any other process to produce a plurality of olive particles. The starting material is then mixed with the polar aqueous solvent, whereby at least a portion of the antioxidant components contained in the starting material will be partitioned in the aqueous phase. The polar aqueous solvent can be water, or a mixture of water and any polar solvent that is water miscible, such as a water-miscible polar organic solvent. Suitable water-

(JA1039(col.6,ln.31-44)).

Cuomo even measures the values of hydroxytyrosol, oleuropein, and tyrosol produced by the disclosed method. Example 4 describes extraction of an olive pulp with water to produce an aqueous solution, which was placed on a column, washed with methanol, and dried to produce a solid. (JA1041-42(col.10,ln.63–

col.11,ln.6)). Example 11 measures the phenolic content of the extract obtained from the process of Example 4. (JA1043(col.14,ln.12-13)). It provides that the dried extract was dissolved in "80% aq. Methanol" and the resulting aqueous solution, containing water-soluble methanol and phenolic compounds, was characterized by HPLC (High Performance Liquid Chromatography). (JA1043(col.14,ln.14-32)). The results of the HPLC analysis are provided in Table 2:

TABLE 2

Assay of Acid-Treated Composition

Assay	Example 4	Example 11
Antioxidant Activity (mM trolox eq./g)	7.64	18.34
Antioxidant Activity (AsA equiv.)	0.61	1.12
Phenols (wt % gallic acid eq.)	16.4	19.8
Hydroxytyrosol (wt. %)	1.09	3.99
Tyrosol (wt. %)	0.5	1.10
Oleuropein (wt. %)	0.4	0.09

This data results in the following ratios, which demonstrate that the solution contains more hydroxytyrosol than oleuropein and tyrosol:

Hydroxytyrosol (wt%)	Oleuropein (wt%)	HT:OE Weight Ratio
3.99%	0.09%	3.99:0.09 = **44.33:1**

Hydroxytyrosol (wt%)	Tyrosol (wt%)	HT:T Weight Ratio
3.99%	1.10%	3.99:1.10 = **3.631**

Cuomo further discloses that "[p]referably, the antioxidant composition is a solid composition. In this aspect, the nutritional supplement can be provided in any convenient form, such as a powder, a tablet or a capsule." (JA1040-41(col.8,ln.66-col.9,ln.2)).

b. Romani, et al., "Polyphenolic Content in Five Tuscany Cultivars of *Olea europaea* L." ("Romani")

Romani, a scientific publication published February 9, 1999, discloses compositions extracted from olive fruits that are high in polyphenols. (JA981). Romani teaches an "aqueous solution" prepared from an extract of ground olive fruit rinsed with acid water, which is further extracted with *n*-hexane to remove lypophilic compounds, resulting in a "defatted aqueous solution." (JA981-82).

Romani analyzes an aqueous solution extracted from five cultivars of olives from Tuscany, and the polyphenolic content in each:

Table 2. Polyphenolic Compounds (Milligrams per Kilogram of Olives) in Different Cultivars[a]

	Cl	Cu	Ro	Gr	Fr
hydroxytyrosol	568.84 ± 28	1049.50 ± 56	4133.00 ± 41	1812.20 ± 51	1694.00 ± 78
tyrosol	101.32 ± 2.3	189.49 ± 4.9	413.13 ± 14	292.75 ± 13	1186.00 ± 92
vanillic acid	6.17 ± 0.8		1.94 ± 0.06	6.45 ± 0.5	2.38 ± 0.1
demethyloleuropein	142.57 ± 4.1	104.95 ± 1.2	13.30 ± 0.3	87.78 ± 5.1	600.30 ± 17
oleuropein	2406.2 ± 87.8	1557.90 ± 60	35.83 ± 0.1	1136.20 ± 10	590.50 ± 58
oleuropein aglycon	1311.9 ± 25.7	1555.80 ± 90	24.19 ± 1.8	1990.60 ± 45	685.20 ± 23
rutin	211.43 ± 3.3	272.96 ± 11	161.43 ± 5.4	146.89 ± 11	111.20 ± 15
luteolin 7-*O*-glucoside	129.13 ± 4.3	69.00 ± 4.8	46.60 ± 2.8	4.75 ± 0.9	60.10 ± 2.1
luteolin	14.00 ± 0.6	11.40 ± 0.9	47.92 ± 2.7	1.04 ± 0.03	29.94 ± 4.9
apigenin 7-*O*-glucoside	40.55 ± 1.6	32.23 ± 2.0	12.67 ± 0.7	29.31 ± 0.7	8.20 ± 0.3
apigenin 7-*O*-rutinoside	17.66 ± 0.4	7.90 ± 0.3	12.84 ± 1.9	3.90 ± 0.4	12.80 ± 1.8
homoorientin	5.64 ± 0.1	3.64 ± 0.3	0.37 ± 0.02	0.53 ± 0.05	1.05 ± 0.06
verbascoside	3202.10 ± 42	939.50 ± 60	551.24 ± 36.4	181.37 ± 2.8	216.20 ± 11
cyanidin 3-*O*-glucoside	282.8 ± 3.5	85.43 ± 1.8	881.72 ± 4.8	65.00 ± 1.7	52.33 ± 1.3
cyanidin 3-*O*-rutinoside	948.00 ± 16.9	399.99 ± 6.6	3205.71 ± 38.8	248.29 ± 4.1	307.33 ± 7.4
total acylated and/or glycoside anthocyans	370.65 ± 15.5	tr[b]	288.10 ± 9.5	252.08 ± 12.2	283.48 ± 13.1

[a] Means ± SD of three determinations. [b] Traces.

The Rossellino cultivar (Ro) reportedly contains 4133.00 mg of hydroxytyrosol and only 35.83 mg of oleuropein, giving a weight ratio of hydroxytyrosol to oleuropein of approximately 115:1. Ro is also reported to contain 413.13 mg of tyrosol, giving a weight ratio of hydroxytyrosol to tyrosol of approximately 10:1. The weight ratio of hydroxytyrosol to tyrosol in three other cultivars (Ciliegino, Cuoricino, and Grossolana) exceeds 5:1. (JA983(Table 2)).

3. The '599 Patent

Like the '808 Patent, the '599 Patent claims require certain ratios of hydroxytyrosol to oleuropein. The '599 Patent focuses on methods of using these compounds to treat specific inflammatory conditions. (JA880). While the specification broadly describes the possible treatment of a number of conditions, claim 1 is narrowly tailored to address only methods of treating coronary, bronchial, or neuro-inflammation:

> **1**. A method of treating a subject having an inflammatory condition characterized by a detectable clinical symptom or change in a level of a biochemical marker with respect to the normal range of the marker, the method comprising:
>
> administering to the subject a dose corresponding to between about 0.1 mg/kg body weight and 2000 mg/kg body weight daily of a first treatment agent comprised of an olive plant extract having a weight ratio of hydroxytyrosol to oleuropein of between about 1:1 and about 200:1; and
>
> continuing said administration until there is observed a return of the marker level to the normal range or a desired change in the clinical symptom,
>
> where the marker or the clinical symptom is selected from the group consisting of
>
> (i) elevated levels of C-reactive protein in the case of coronary inflammation;
>
> (ii) respiratory distress in the case of bronchial inflammation; and
>
> (iii) elevated CSF levels of isoprostanes or clinical symptoms determined from neuropsychological testing in the case of neuro inflammation.

The second independent claim of the '599 Patent is similarly limited to treatment of specific conditions:

> **16**. A method of treating an inflammatory condition in a subject in need of such treatment, comprising administering to said subject a dosage amount corresponding to between about 0.1 mg/kg body weight and 2000 mg/kg body weight daily of substantially purified hydroxytyrosol or a substantially purified mixture of hydroxytyrosol and oleuropein, wherein said inflammatory condition is in response to a condition selected from the group consisting of: delayed type hypersensitivity reaction, psoriasis, an autoimmune disease, organ transplant, pain, fever, and tissue graft rejection.

Claim 16 does not require a specific weight ratios, but instead requires that the method of treatment include administration of substantially purified

hydroxytyrosol or a substantially purified mixture of hydroxytyrosol and oleuropein.

The '599 Patent specification provides no data to support the anti-inflammatory effects of the claimed olive-derived preparations. Instead, the specification provides four examples that are intended to "illustrate the invention." (JA90(col.16,ln.37-38)). Each example, however, merely describes testing that the alleged inventor, Dr. Roberto Crea, intended to do, but either had not yet started or had not yet completed at the time he filed the patent application. Not one of these examples describes any test establishing that hydroxytyrosol-rich compositions, as described in the claims, could be used to treat any of the claimed inflammatory conditions. The only suggestion of results prior to filing the patent application that led to the '599 Patent are "initial results" relating to isoprostane levels in urine, as opposed to the claimed CSF levels. (JA91(col.18,ln.36-38)). The patent does not describe any data regarding C-reactive protein, respiratory distress, or elevated CSF levels of isoprostanes. Moreover, there is no actual data reported and the sample size indicated is only "up to 32 subjects." (JA893(col.18,ln.7-8)). The specification does not provide any data relating to any change in inflammation caused by delayed type hypersensitivity reaction, psoriasis, an autoimmune disease, organ transplant, pain, fever, or tissue graft rejection.

B. Procedural History

1. Pleadings and Request for Reexamination

CreAgri filed this action on December 23, 2011. (JA39(DN1)). CreAgri has admitted that it brought this lawsuit without buying or testing any of Pinnaclife's products. (JA942-43). Despite the lack of test results, CreAgri alleged that Pinnaclife "has infringed and continues to infringe" the '808 Patent through its sale of dietary supplements containing olive-derived compounds. Nowhere does CreAgri describe the basis for its allegation that the Pinnaclife products meet the specific claimed ratios of compounds found in the patents-in-suit.

On July 24, 2012, Pinnaclife submitted a Request for Reexamination of the '808 Patent to the U.S. Patent & Trademark Office ("USPTO") on the ground that the claimed weight ratios had been disclosed in the prior art, including Cuomo and Romani. That request was granted, reexamination commenced, and the examiner issued a Final Office Action on November 8, 2013, rejecting all claims of the '808 Patent. (JA54(DN140)). Following a January 17, 2014, Advisory Action, CreAgri appealed. The reexamination remains pending on appeal, and a Certificate of Reexamination has not yet issued.

Pinnaclife sent CreAgri a copy of the Request before it was submitted and attempted to meet and confer, but following no substantive response from CreAgri, Pinnaclife submitted the Request for Reexamination to the USPTO on July 24,

2012. Six days later CreAgri filed an Amended Complaint reasserting its allegations of infringement of the '808 Patent and alleging for the first time that Pinnaclife's dietary supplements infringed the '599 Patent. (JA41(DN23)).

Following a successful Motion to Dismiss CreAgri's Amended Complaint on the grounds that it failed to allege facts supporting its indirect infringement claims, CreAgri filed a Second Amended Complaint ("SAC") on January 22, 2013. (JA43-44(DN46,50)). CreAgri's SAC again failed to provide any factual basis for its allegation that Pinnaclife's dietary supplement products fall within the weight ratios or level of purification required by the claims of either patent.

2. Claim Construction Proceedings

Following thorough briefing by both Parties, the court held a full-day *Markman* hearing on February 8, 2013, during which the parties addressed their proposed constructions of multiple terms appearing in the '808 and '599 Patent claims. Among those disputed claim terms was "aqueous extract of olives," which the parties proposed to construe as follows:

Term in Dispute	CreAgri's Proposed Construction	Pinnaclife's Proposed Construction
"aqueous extract of olives"	"a water-soluble preparation from an olive plant"	"an aqueous solution containing water-soluble compounds obtained by washing and pressing olive fruit"

(JA38.23). Pinnaclife initially sought a construction that "'an aqueous extract' is not an 'aqueous-alcoholic extract'" but reconsidered this construction during briefing and removed that requirement. (JA364). CreAgri did not object and

made no attempt to revise its own proposed construction to exclude "aqueous-alcoholic extracts."

On April 16, 2013, the district court issued a detailed order construing the disputed terms, including "aqueous extract of olives" to mean "'an aqueous solution containing a water-soluble preparation from an olive plant,' with no restriction on the process by which the 'aqueous solution' is obtained." (JA38.40). CreAgri did not object to this construction following the claim construction hearing.

3. Summary Judgment

On September 19, 2013, the parties filed cross-motions for summary judgment. (JA832,JA1113). CreAgri moved for summary judgment of infringement asserting that the accused products satisfy every limitation of the asserted claims in the '808 Patent, and that Pinnaclife performs and induces performance of every step of the asserted claims of the '599 Patent. (JA1113). In its Opposition, Pinnaclife presented undisputed facts establishing that the accused products contain more oleuropein than hydroxytyrosol, and that the products are powders—not aqueous solutions. (JA51(DN11-1)).

Pinnaclife moved for summary judgment of invalidity under 35 U.S.C. §§ 102 and 103 on the grounds that all claims of the '808 Patent are anticipated or rendered obvious by prior art, principally relying on Cuomo and Romani.

Pinnaclife also argued invalidity on the basis that the '808 Patent impermissibly claims non-patentable subject matter under 35 U.S.C. § 101, and that the '808 Patent and '599 Patent fail the written description and enablement requirements of 35 U.S.C. § 112 and lack utility under 35 U.S.C. § 101. (JA832).

On December 18, 2013, the court issued a thorough opinion declaring both patents-in-suit invalid and determining that it need not reach the cross-motions on infringement. (JA3). All remaining claims and counterclaims were dismissed without prejudice as moot, and Judgment was entered in favor of Pinnaclife on January 3, 2014. (JA37).

The district court declared the '808 Patent invalid as anticipated under 35 U.S.C. § 102 and the '599 Patent invalid for failure to meet the written description, enablement, and utility requirements of 35 U.S.C. §§ 101 and 112(a). As to anticipation of the '808 Patent, the court held that "claims 1-5 of the '808 Patent are invalid as anticipated by Cuomo." (JA10). The court concluded "that Example 11's description of an 80% *aqueous* methanol solution comprising the dissolved olive pulp from Example 4 plainly describes an 'aqueous solution containing a water-soluble preparation from an olive plant,' and therefore no reasonable jury could conclude that the reference fails to disclose the 'aqueous extract of olives' limitations of claims 1 through 5 of the '808 Patent." (JA11).

In addition, the court rejected as waived CreAgri's attempt to relitigate the construction of "aqueous extract" at the summary judgment stage, but in any event found that CreAgri's newly-proposed claim construction argument that "aqueous extract" excluded "aqueous-alcoholic extracts" failed on the merits. (JA11-12). The court found that the "specification of the '808 Patent makes clear that the invention includes—rather than excludes—the use of aqueous-alcoholic extracts." (JA12). And, "[b]ecause the patentee described the invention as being formulated from aqueous-alcoholic extracts, [the] Court refuse[d] to exclude aqueous-alcoholic extracts from the scope of the 'aqueous extract' claim language." (JA13).

The court also found that Pinnaclife had established the absence of an issue of material fact as to the anticipation of claims 1-2 and 5-6 by Romani because Romani discloses the weight ratios of those claims and "[b]oth the 'aqueous solution' and the defatted 'aqueous phase' [disclosed in Romani] plainly constitute an 'aqueous extract of olives' under the Court's claim construction." (JA15).

The court declared the '599 Patent invalid for failure to meet the written description requirement of section 112 on the basis that "the cited prior art does not suggest that persons having ordinary skill in the art would understand the specification's disclosure to describe that the inventor invented what was claimed." (JA28). The court further held "[t]he study outlines disclosed in the specification

itself all reveal that the inventor's statements of invention are, at best, premature" and "[t]he written description requirement prohibits inventors from preempting the future before it has arrived." (*Id.*).

The court also found all the '599 Patent claims invalid for failure to meet the enablement requirement of section 112 because "Pinnaclife has satisfied its burden of establishing that no reasonable jury could conclude that a person of ordinary skill in the art would accept without question the general assertion that olive-derived phenols would effectively treat the various forms of inflammation as recited in the claims." (JA35). The court further found the '599 Patent lacked utility under 35 U.S.C. § 101 because "it does not explicitly provide any analytic reasoning as to why the invention would work as claimed." The invention is not patentable because "[t]he '599 Patent does not claim a therapy, it claims a research hypothesis." (JA36).

SUMMARY OF THE ARGUMENT

The judgment declaring the '808 and '599 Patents invalid is supported by the law and the record and should be affirmed in its entirety.

In appealing the district court's declaration that the '808 Patent is invalid as anticipated, CreAgri relies on a belated claim construction position deemed waived by the district court. But CreAgri does not appeal—or even mention—the court's finding of waiver. The finding of waiver is thus not before this Court. But even if it was, the court did not abuse its discretion in deeming CreAgri's untimely claim construction position waived and rejecting it. Even absent waiver, CreAgri's newly proposed construction of "aqueous extracts" as excluding "aqueous-alcoholic extracts" is not supported by the '808 Patent. Under either construction, Cuomo and Romani disclose an "aqueous extract of olives" and thus anticipate the '808 Patent claims. The court's finding that the '808 patent is invalidated as anticipated must be affirmed.

The court also correctly found the '599 Patent invalid under 35 U.S.C. § 112 for failing the written description and enablement requirements and under 35 U.S.C. § 101 for lack of utility because CreAgri presented no evidence that the claimed treatment agents had any effect *on the claimed inflammatory conditions*. Rather, the specification revealed nothing more than the inventor's hope that olive-derived compositions would one day be used to treat inflammation caused by a

wide variety of factors. The court's findings declaring the '599 Patent invalid under sections 112 and 101 should be affirmed.

STANDARD OF REVIEW

A decision to grant or deny summary judgment is reviewed *de novo*, and on appeal, the reviewing court applies the same standard used by the trial court. *Jones v. Blanas*, 393 F.3d 918 (9th Cir. 2004); *see also Taurus IP, LLC v. Daimler Chrysler Corp.*, 726 F.3d 1306,1322 (Fed. Cir. 2013) (regional circuit law applies to review of summary judgment grant). Summary judgment is as appropriate in a patent case as in any other. *Nike, Inc. v. Wolverine World Wide, Inc.*, 43 F.3d 644, 646 (Fed. Cir. 1994). The Court should grant summary judgment "where, drawing all reasonable inferences in favor of the non-movant, there is no genuine issue as to any material fact and no reasonable jury could return a verdict for the non-movant." *Roche Palo Alto LLC v. Apotex, Inc.*, 531 F.3d 1372, 1377 (Fed. Cir. 2008); *see also* Fed. R. Civ. P. ("FRCP") 56(a).

"Because a patent is presumed to be valid, *see* 35 U.S.C. § 282 (1994), the party asserting invalidity has the burden of showing invalidity by clear and convincing evidence." *WMS Gaming, Inc. v. Int'l Game Tech.*, 184 F.3d 1339, 1355 (Fed. Cir. 1999). When the moving party meets its burden, the opposing party must set forth specific facts showing a genuine issue of material fact. FRCP 56(c). Here, there are no disputed facts because the basis for summary judgment is contained within the patents and prior art references.

A claim is anticipated where "each and every limitation is found either expressly or inherently in a single prior art reference." *Bristol-Myers Squibb Co. v. Ben Venue Labs, Inc.*, 246 F.3d 1368, 1343 (Fed. Cir. 2001). Anticipation under 35 U.S.C. § 102 is a two-step inquiry. *Medichem, S.A. v. Rolabo, S.L.*, 353 F.3d 928, 933 (Fed. Cir. 2003). The first step is a proper construction of the claims, which is reviewed *de novo*. *Id.* The second step requires a comparison of the properly construed claim to the prior art. *Id.* Anticipation is "a question of law to be determined based upon underlying factual determinations." *Eiselstein v. Frank*, 52 F.3d 1035, 1038 (Fed. Cir. 1995).

"[A] patent can be held invalid for failure to meet the written description requirement, based solely on the language of the patent specification." *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927 (Fed. Cir. 2004). If no reasonable juror could find that a patentee's disclosure was sufficiently detailed to enable one of skill in the art to recognize that the patentee invented what the patent claimed, then a grant of summary judgment of invalidity is appropriate. *Id.* "Compliance with the written description requirement is a question of fact but is amenable to summary judgment in cases where no reasonable fact finder could return a verdict for the non-moving party." *PowerOasis, Inc. v. T-Mobile USA, Inc.*, 522 F.3d 1299, 1307 (Fed. Cir. 2008).

"Lack of enablement and absence of utility are closely related grounds of unpatentability." *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350, 1358 (Fed. Cir. 1999). Utility is an issue of fact. *Id.* Enablement is a question of law, which this Court reviews "*de novo*, deferring to its assessment of subsidiary facts underlying the legal question unless clearly erroneous." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1334 (Fed. Cir. 2003) (internal citations omitted).

ARGUMENT

I. The District Court Correctly Construed "Aqueous Extract of Olives."

CreAgri urges this Court to reverse the district court's declaration of invalidity of the '808 Patent based on purported reversible error in the court's construction of "aqueous extract of olives"—a term appearing in both independent claims. (CA16-17). CreAgri's argument fails on numerous grounds. First, CreAgri did not appeal the district court's finding that its new claim construction argument at the summary judgment stage was untimely, had been waived, and therefore must be rejected. Second, even if CreAgri had appealed the finding of waiver, the court did not abuse its discretion in finding that CreAgri waived its new claim construction argument. Third, if this Court nevertheless decides to review the court's construction, CreAgri's current proposed construction that "aqueous

extracts" should exclude "aqueous-alcoholic extracts" is unsupported by the intrinsic record.

A. CreAgri Waived Its Right To Appeal the Finding of Waiver.

CreAgri does not even mention much less appeal the district court's finding that its "argument is a new and untimely claim construction argument" and its "attempt to relitigate the construction of 'aqueous extract' at the summary judgment stage must be rejected." (JA11-12). Accordingly, the court's finding that CreAgri waived its new claim construction argument should be affirmed. *Greenwood v. FAA*, 28 F. 3d 971, 977 (9th Cir. 1994) ("We review only issues which are argued specifically and distinctly in a party's opening brief. . . . [J]udges are not like pigs, hunting for truffles buried in briefs.") (internal quotations omitted); *SmithKline Beecham Corp. v. Apotex Corp.*, 439 F.3d 1312, 1319 (Fed. Cir. 2006) (same). Here, CreAgri completely ignores the court's finding of waiver—arguably misleading this Court by failing to even mention it. CreAgri's appeal should therefore be rejected for failure to appeal a necessary component of the judgment.

B. The District Court Did Not Abuse Its Discretion in Finding that CreAgri Waived Its New Claim Construction Argument.

Even if CreAgri had appealed the finding of wavier, the court did not abuse its discretion in finding that CreAgri waived its new claim construction argument and could not raise it during summary judgment. *See Nikko Materials USA, Inc. v.*

NavCom Def. Elecs., Inc., 534 Fed Appx. 656, 657n.1 (9th Cir. 2013) ("[A] district court's conclusion regarding discretionary waiver of an issue or claim by failure to timely assert it in litigation" is reviewed for "abuse of discretion."); *F.Lii de Cecco di Filippo Fara S. Martino S.P.A. v. U.S.*, 216 F.3d 1027, 1031 (Fed. Cir. 2000) ("[E]videntiary decisions, including waiver for failure to timely present evidence or raise an issue, are reviewed for abuse of discretion.").

During claim construction, CreAgri proposed a broad construction for "aqueous extract of olives," asking the court to construe that term as meaning "a water-soluble preparation from an olive plant."[1] (JA11-12;JA254). In its order construing disputed claim terms, the court adopted a strikingly similar construction, defining "aqueous extract" as "an aqueous solution containing a water-soluble preparation from an olive plant." (JA38.30). But despite the fact that the court largely adopted CreAgri's proposed construction, CreAgri ignored these findings and argued for the first time during summary judgment—more than five months after the claim construction order—that "a liquid extract that includes methanol…cannot be an aqueous extract, even if that extract also includes water." (JA11). In other words, CreAgri asserted a more narrow construction of the

[1] CreAgri does not dispute that "aqueous-alcoholic extracts" are water-soluble, which would run contrary to its current and former claim construction positions, as well as basic science.

disputed term to assert that "'aqueous extracts' are not meant to encompass 'aqueous-alcoholic extracts.'" (JA2369).

The court did not abuse its discretion in rejecting CreAgri's new construction during this late stage of the litigation. Indeed, this Court has repeatedly emphasized the importance of seeking an appropriate construction of disputed terms in the claim construction phase. In *Enovsys LLC v. Nextel Communications, Inc.*, this Court deemed a claim construction argument waived where "neither party objected to how the district court construed" a limitation or sought a "more specific definition" of the limitation. 614 F.3d 1333, 1339, 1344 (Fed. Cir. 2010). Similarly, in *Eli Lilly & Co. v. Aradigm Corp.*, this Court rejected as waived Aradigm's attempt to seek additional claim construction after the close of evidence at trial. 376 F.3d 1352, 1360 (Fed. Cir. 2004).

The present case is not precisely analogous to *Enovsys* or *Aradigm*, where waiver resulted from a failure to seek a construction of the disputed term. The circumstances here are much more egregious. CreAgri not only failed to object to the court's construction, but CreAgri *itself* essentially proposed the construction it now seeks to narrow. CreAgri at no time sought a construction of "aqueous extract" that would exclude "aqueous-alcoholic extracts." It urged the court to adopt a broad construction covering all water-soluble olive-derived compositions.

Had CreAgri intended to seek a more specific definition of "aqueous extract" during claim construction, it easily could have done so. CreAgri's waiver is even more evident in light of Pinnaclife's initial proposed construction that would have limited "aqueous extract" by excluding aqueous-alcoholic extracts. (JA584). Pinnaclife ultimately withdrew its proposal and removed that requirement. (JA364). CreAgri did not object. Nor did it attempt to revise its proposed construction to exclude aqueous-alcoholic extracts. CreAgri's waiver is thus clear. It was aware of this alternate proposed construction and had the opportunity at the time of the claim construction phase to advance its current position. It failed to do so.

CreAgri was also aware of the relevant prior art references as Pinnaclife asserted Cuomo and Romani in its invalidity contentions and Request for Reexamination. But only after Pinnaclife raised them during summary judgment did CreAgri abruptly changed its claim construction position. The court properly rejected CreAgri's new construction because CreAgri waived any claimed error associated with the construction of "aqueous extract" by asserting essentially the construction ultimately adopted by the district court and failing to request any more specific definition.

C. The District Court Did Not Err in Its Construction of "Aqueous Extract of Olives."

Even if waiver did not apply, CreAgri's recently-devised claim construction position fails on the merits. CreAgri relies entirely on the use of the term "or" separating "aqueous" and "aqueous alcoholic" in an attempt to differentiate those two terms. (CA21). But this position is inconsistent with the use of "aqueous extract" and "aqueous-alcoholic extract" in the '808 patent. The use of "or" does not redefine "aqueous-alcoholic extract" as anything other than its plain meaning—a subset or species of the broader "aqueous extract" genus. That is, an "aqueous-alcoholic extract" is simply one type of an "aqueous extract."

Moreover, as CreAgri previously urged, both "aqueous" and "aqueous-alcoholic" extracts are "simply water soluble." (JA255 ("Thus, as well understood in the art and disclosed in the '808 Patent, an aqueous extract is simply an extract that is soluble in the aqueous phase, or water soluble."); JA559). Indeed, the term "aqueous extract" does not mean that the extract only contains water. Rather, it is the hydrophilic layer of an extraction, as opposed to the hydrophobic layer. CreAgri's new reading of these two terms in the disjunctive is illogical. This Court should affirm the construction applied by the district court as neither the specification nor the claims support CreAgri's proposed construction.

1. "Or" Does Not Unequivocally Describe Mutually-Exclusive Alternatives.

CreAgri's reliance on two decisions to assert that "or" must unequivocally describe mutually-exclusive alternatives fails. In *SkinMedica* and *Joy* (an unpublished and non-precedential case), the patents-at-issue explicitly distinguished between two alternatives connected by "or" in the disjunctive sense. Neither case relied solely on the use of "or" to find mutual exclusivity in alternative terms as CreAgri does.

In *SkinMedica*, this Court considered whether a patentee's specification defining cell culture methods should be interpreted to differentiate between "cells are cultured in monolayer, beads (i.e. two-dimensions) or, preferably, in three dimensions." *SkinMedica, Inc. v. Histogen Inc.*, 727 F.3d 1187,1199 (Fed. Cir. 2013). At issue was whether "beads (i.e. two dimensions)" and "three dimensions" referred to mutually-exclusive alternative culture methods, where the plain meaning of "beads" suggests a three-dimensional structure. *Id.* at 1196. The Court did not rely solely on the use of the disjunctive "or," but instead looked to whether redefinition of a term using two terms as alternatives was clear and explicit in the specification. *Id.* at 1200. The Court ultimately found that "the inventors clearly expressed intent to differentiate the use of beads from three-dimensional culturing" based on both the express reference to "i.e. two dimensional" in the definitional

sense and repeated consistent use of the term "beads" in that manner throughout the specification. *Id.* at 1201.

Similarly, the Court in the non-precedential *Joy* opinion found a lack of evidence in the specification that the inventor "intended for the definition of…'indentations' to extend beyond its ordinary meaning to include holes." *Joy MM Delaware, Inc. v. Cincinnati Mine Machinery Corp.*, 497 Fed. Appx. 970, 973 (Fed. Cir. 2012). While the Court looked to the inventor's use of the disjunctive "or," it did so in the context of confirming the exclusion of "holes" from the plain meaning of "indentations." *Id.*

These cases make clear that the use of "or" does not, in and of itself, demonstrate an inventor's explicit and unambiguous intent to alter the ordinary meaning of a claim term. Here, the terminology alone demonstrates that the plain meaning of "aqueous-alcoholic" falls within the scope of "aqueous." The inventor expressed no clear or explicit intent to redefine "aqueous" as excluding "aqueous-alcoholic." Contrary to CreAgri's assertions, the mere use of "or" between these two terms in two paragraphs of the '808 patent specification is not sufficient to establish that "aqueous-alcoholic extracts" are anything other than a subset of the broader group "aqueous extracts."

2. The Intrinsic Record Supports the Court's Construction.

In support of its new construction, CreAgri asserts that the court improperly relied on a passage in the specification describing oral dosage forms including both "aqueous" and "aqueous-alcoholic" extracts as indicative of the invention as a whole. (CA24-25;JA12). Regardless of its rationale, however, the court held that "the specification's passing use of the disjunctive to connect overlapping adjectives is ambiguous at best." (JA13;CA26). This is consistent with the holdings of *SkinMedica* and *Joy*, which require an inventor to redefine a term only through explicit and unambiguous language in the specification. The '808 Patent's inventor plainly failed to set forth any language—explicitly or otherwise—that could be interpreted to exclude "aqueous-alcoholic" from being a form of an "aqueous" extract.

CreAgri argues that the court should have resolved the "ambiguity" in the specification's use of "or" "in such a way to maintain the validity of the '808 Patent." CreAgri cites yet another unpublished case, *Medtronic Navigation, Inc. v. BrainLab Medizinische Computersysteme GmbH*, 222 Fed. Appx. 952, 956 (Fed. Cir. 2007), to assert that claims "are best construed to preserve their validity." (CA26). But CreAgri misrepresents that holding and it is inapposite. This is not a case where the construction excludes preferred embodiments, or where the written description cannot justify the breadth of the claims, in which case courts may

resolve ambiguity in favor of maintaining validity of a patent, as in *Medtronic*. Rather, the court here declared CreAgri's claims invalid after applying anticipatory references based on a construction that CreAgri essentially proposed and ultimately obtained from the court. Adopting CreAgri's new construction of "aqueous extract" would effectively exclude all "aqueous-alcoholic extracts" described in the specification from the scope of the invention. As the court recognized, imposing such an exclusion would improperly limit the scope of the claims. (JA13). Any ambiguity here must be resolved in favor of a broad construction.

Finally, to the extent CreAgri relies on the process of producing vegetation water described in the specification, that too is unavailing. (CA25-26). The court expressly adopted CreAgri's proposed construction of the term "aqueous extract of olives" to be "with no restriction on the process by which the 'aqueous solution' is obtained." (JA38,40). CreAgri does not challenge this portion of the construction, and its attempt to limit the scope of the claims in light of the process of preparation fails. CreAgri never proposed a construction that would limit "aqueous extract" to vegetation water, as it apparently seeks to do here.

II. The Prior Art Anticipates All Claims of the '808 Patent.

Applying the proper construction of "aqueous extract of olives," the district court correctly held all claims of the '808 patent anticipated by Cuomo and

Romani. In challenging that decision, CreAgri argues that neither reference anticipates because the starting material is not an "aqueous (waste water) extract." (CA27,CA33). CreAgri again ignores the properly-applied construction and strains to create a question of fact where none exists. But even under CreAgri's newly-proposed construction, the '808 Patent is invalid as anticipated by Cuomo and Romani. Accordingly, this Court should affirm the judgment that all claims of the '808 patent are invalid as anticipated.

A. Cuomo Anticipates Claims 1-5 of the '808 Patent.

There is no dispute that Cuomo qualifies as prior art under 35 U.S.C. § 102(e).[2] As detailed above, Cuomo's specification and examples disclose the method of collecting olive wastewater and acidification described in the '808 Patent, and measure the values of hydroxytyrosol, oleuropein, and tyrosol produced by this method. It is undisputed that those compositions—falling within the weight ratios claimed in the '808 Patent—anticipate claims 1-5. (JA10). Thus,

[2] Cuomo qualifies as prior art under 35 U.S.C. § 102(e), which precludes issuance of a patent where "the invention was described in…a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent…." The application leading to Cuomo was filed on December 20, 1999, months before the undisputed earliest date of invention for the '808 patent, May 8, 2000. (JA1029,JA997). Although § 102 was revised by the America Invents Act, the former § 102(e) should apply here. *See Taurus IP, LLC v. DiamlerChrysler Corp.*, 726 F.3d 1306, 1319n.7 (Fed. Cir. 2013). Under the old or new law, Cuomo is prior art.

the only issue for the Court to resolve is whether Cuomo discloses the limitation "aqueous extract of olives." (JA10). There can be little doubt that it does.

1. Cuomo Repeatedly Discloses an "Aqueous Extract of Olives."

The district court defined "aqueous extract of olives" as "an aqueous solution containing a water-soluble preparation from an olive plant," with no restriction on the process by which the "aqueous solution" is obtained. (JA38.40). Cuomo expressly describes such an "aqueous extract of olives."

Specifically, the Field of Invention of Cuomo discloses antioxidant-rich compounds derived "from fresh olives, from olive pulps produced as a by-product of olive oil manufacturing, from olive oil, and from wastewater from olive oil manufacturing." (JA1037(col.1,ln.11-17)). The wastewater, or other olive-based starting material, may be extracted with a polar aqueous solvent—such as water—to produce an aqueous phase. (JA1038(col.4,ln.30-44); JA1041(col.9,ln.35-41)). After extraction of the aqueous phase, the solvent is optionally partially or substantially removed to form either a liquid concentrate or a solid antioxidant composition. (JA1038(col.4,ln.39-41); JA1040(col.8,ln.25-32; JA1041(col.9,ln.42-45)). The aqueous extract may also undergo an acidification procedure to improve the extraction efficiency of antioxidant components. (JA1040(col.7,ln.17-30; col. 9,ln.45-50)).

Cuomo clearly discloses an "aqueous solution containing a water-soluble preparation from an olive plant." In fact, Cuomo specifically describes an aqueous solution in reference to the olive wastewater used in the disclosed process:

> As discussed above, one step of the conventional olive oil production process includes making a slurry of olive solids, olive oil, and water. The water and olive oil are pressed out of the slurry and separated, then the oil is separated from the water by decantation or centrifugation. This "water", referred to herein as "wastewater", is actually a solution of water-soluble antioxidant components, possibly along with small amounts of other materials left over from the olive oil manufacturing process. In this embodiment, this wastewater is used as the starting material in a method of preparing an antioxidant composition. Thus, it is a particular advantage of

(JA1041(col.9,ln.24-30)). Both the wastewater itself and extracts from other olive material are referred to throughout the specification as the "aqueous phase." (JA1029(Abstract),JA1038(col.4,ln.35), JA1039(col.5,ln.60; col.6,ln.32,42), JA1040(col.7,ln.1-29), JA1041(col.9,ln.35)).

Example 4 describes extraction of olive pulp with water to produce an aqueous solution that is subsequently placed on a column, washed with methanol, and dried to solid form. (JA1041-42(col.10,ln.63-col.11,ln.6). Example 11 measures the phenolic content of the extract obtained from the process of Example 4, which is dissolved in "80% aq. methanol." (JA1043(col.14,ln.14)). The

aqueous solution, containing water-soluble methanol and phenolic compounds, is characterized by HPLC, the results of which show the phenolic weight ratios falling within the scope of the '808 Patent claims. (JA1043(Table 2)).

Cuomo plainly describes an "aqueous solution containing a water-soluble preparation from an olive plant," both through repeated disclosure throughout the specification and, more specifically, by its testing of an 80% *aqueous* methanol solution comprising olive-derived components as set forth in Example 11. Cuomo thus satisfies the "aqueous extract of olives" limitation required by claims 1-5 of the '808 patent and was appropriately found to anticipate those claims.

2. Cuomo Anticipates the '808 Patent Claims Under CreAgri's Old and New Claim Constructions.

CreAgri disingenuously attempts to mischaracterize Example 4 as a methanol extraction by glossing over the starting material for Example 4, which uses "[a] 148.48 g sample of the [olive] mash was extracted with water (300 mL) at a reflux temperature for 1 hour." (CA28;JA1041(col.10,ln.65-67)). This aqueous extraction serves to dissolve water-soluble olive-derived components, including hydroxytyrosol, tyrosol, and oleuropein, in water. Example 4 describes a series of purification steps, where the aqueous solution is further washed with methanol and filtered. These steps do not change the phenolic content of the composition subsequently analyzed in Example 11. CreAgri's reliance on a

methanol wash in an attempt to place Cuomo outside the scope of the claims is unsupported.

CreAgri's assertion that Cuomo does not anticipate even under the court's construction of "aqueous extract of olives" is wrong. (CA27). CreAgri's argument on appeal is identical to that made before— and rejected by—the district court. (JA12-13). CreAgri contends it presented a genuine issue of material fact as to anticipation "because it presented evidence that the source material used in Example 11 of Cuomo is derived from an alcohol extract and could not be converted to aqueous after the fact." (CA30). This argument is conceptually and technically wrong. First, CreAgri confuses the steps taken to purify the extract for analysis with the extraction process itself. The fact that extracted antioxidant material was purified using a solid matrix column and a methanol wash does not negate the fact that the same hydroxytyrosol, oleuropein, and tyrosol are first found in an aqueous extract. Second, the antioxidant composition is thereafter dissolved in 80% *aqueous* methanol, loaded onto an HPLC column for analysis, and eluted with an aqueous solution. Thus, at the precise time the phenolic content is measured by HPLC, the sample is in fact "an aqueous solution containing a water-soluble preparation from an olive plant."

CreAgri continues its misleading argument by asserting that Example 11 of Cuomo analyzes "a aqueous-alcoholic ***solution*** made from an alcohol extraction of

olives." (CA32(emphasis supplied)). Not only does CreAgri mischaracterize the composition of Example 4 as an alcohol extraction, but CreAgri's own incorrect interpretation falls squarely within the court's construction of "aqueous extract of olives." Even relying on CreAgri's own misinterpretation, the composition of Example 11 is "an aqueous solution containing a water-soluble preparation from an olive plant," whether that solution is made from an alcohol extraction or otherwise. Indeed, CreAgri cannot claim such an aqueous-alcoholic solution is a water-insoluble preparation. And, in any event, the court's expressly declined to limit an "aqueous extract of olives" to a specific process by which the solution is made. (JA38.40). Under either interpretation, Cuomo discloses an "aqueous extract of olives" containing the weight ratios specified in claims 1-5 of the '808 patent.

3. CreAgri Fails To Create a Disputed Issue of Fact.

CreAgri contends that Pinnaclife did not meet its burden because it relied solely on attorney argument. (CA32-33). This is entirely inaccurate as Pinnaclife relied on the undisputed facts described in the reference itself.

CreAgri relies on a single paragraph of Dr. German's expert report to assert that rinsing a column with methanol amounts to production of a methanolic extract. (CA30). But that paragraph of the report, in reality, states only that organic solvents are not "aqueous extracts," and does not in any way address the alcoholic extraction that CreAgri argues here. (JA2420-21). More egregiously, as

recognized by the court, "Dr. German fails even to acknowledge that Example 11 expressly analyzes an *aqueous* methanol solution for phenolic content." (JA13). Dr. German incorrectly interpreted Cuomo as analyzing the phenolic content of a *solid* composition, where Example 11 plainly states otherwise. (JA1000-01).

CreAgri cites two cases in support of its argument that Pinnaclife must present expert opinion to succeed on its invalidity position, both of which are clearly distinguishable. In *Crown Packaging Technology, Inc. v. Rexam Beverage Can Co.*, 559 F.3d 1308, 1315 (Fed. Cir. 2009), this Court did not rely on the purportedly improper use of attorney argument in place of evidence, but instead held that rebuttal evidence unrecognized by the court created a material issue of fact. *Id.* That is not the case here, where the court closely evaluated the CreAgri's expert's opinion and found it woefully incomplete. (JA13-14).

In *Elcommerce.com, Inc. v. SAP AG*, 745 F.3d 490 (Fed. Cir. 2014), this Court held that the invalidity determination lacked an evidentiary basis because the court requested, but failed to receive, expert opinion needed to determine what structure corresponds to a means-plus-function limitation. *Id.* at 503. Notably, this Court expressly recognized that expert opinion is not always required: "We do not of course hold that expert testimony will always be needed for every situation; but we do hold that there is no Federal Circuit or other prohibition on such expertise." *Id.* at 506. Accordingly, neither case requires Pinnaclife to present expert opinion

to rebut the incomplete and inadequate opinion of CreAgri's expert that plainly fails to present a genuine issue of material fact, particularly in light of the undisputed facts expressly disclosed in the prior art.

Cuomo clearly and convincingly anticipates claims 1-5 of the '808 patent. The judgment declaring the '808 patent invalid in light of Cuomo should be affirmed.

B. Romani Anticipates Claims 1-2 and 5-6 of the '808 Patent.

Romani qualifies as prior art under 35 U.S.C. § 102(b)[3] and discloses olive extracts having the phenolic weight ratios required by the '808 Patent claims. As with Cuomo, the only issue for determination by this Court is whether Romani discloses an "aqueous extract of olives." It does.

1. Romani Discloses an "Aqueous Extract of Olives."

Romani teaches an "aqueous solution" prepared from an extract of ground olive fruit rinsed with acid water. (JA981). In preparing samples of five olive cultivars, Romani describes mixing frozen olive pulp with aquesou-alcohol (80% ethanol), rinsing the mix with acid water, then removing the fat-soluble molecules with n-hexane to produce an "aqueous phase." (JA981-82). The "defatted

[3] Section 102(b) precludes issuance of a patent where "the invention was patented or described in a printed publication in this or a foreign country . . . more than one year prior to the date of application for a patent in the United States." Romani published on February 9, 1999—well over one year before the May 8, 2000 earliest possible date of invention for the '808 patent. (JA981,JA997).

aqueous solution" is then described as undergoing a series of elution steps, concentration, and analysis by HPLC. (JA982). Romani further reports the use of 100% water as a solvent for the olive extract analyzed by HPLC. (JA982) ("A four-step linear solvent gradient was used, starting from 100% H_2O . . ."). These steps expressly describe both an "aqueous solution" and an "aqueous phase" derived from an olive plant. The methods of preparation thus plainly disclose "an aqueous solution containing a water-soluble preparation from an olive plant," and the "aqueous extract of olives" limitation of each claim is satisfied by Romani.

2. Romani Anticipates Under CreAgri's New Construction.

Romani expressly discloses olive material, rinsed with a number of solvents including 80% ethanol, acid water, ethyl acetate and methanol, then dried to form a solid. (JA982). That solid—containing the olive-derived phenols that Romani aimed to characterize—is subsequently dissolved in 100% water and analyzed via HPLC. (JA982 ("The eluent was H_2O…starting from 100% H_2O")). The solution comprising water and olive-derived phenols no longer contains alcoholic solvents, which have been removed by evaporation. (JA982). That solution containing water-soluble phenolic compounds measured and reported by Romani is an "aqueous extract of olives," even under a construction that excludes "aqueous-alcoholic extracts."

3. The District Court Properly Found Anticipation By Romani.

Romani also discloses an "aqueous extract of olives" under the district court's construction. As recognized by the court, Romani expressly discloses both an "aqueous solution" and an "aqueous phase," and the content of phenols dissolved in water is measured directly. (JA981-982). Ignoring that express disclosure, CreAgri argues that the court made an "assumption" that the process of measuring the phenolic content does not alter the levels of the measured phenols found in the olive. (CA36). This argument mischaracterizes the court's order, which relies upon the Romani reference itself. (JA16).

After concluding that Romani expressly discloses an "aqueous extract of olives," the court noted that:

> Romani does not suggest, and CreAgri does not contend, that the polyphenolic profiles change depending on the phase of the described olive extracts. To the contrary, Romani discloses using the dry fractions to determine the polyphenolic content of the original olive. The premise of this procedure is that the intermediate steps in the measurement process (during which the authors obtain the aqueous extract of olives) do not alter the hydroxytyrosol, tyrosol, and oleuropein levels naturally found in the Rossellino cultivar, levels that indisputably fall within the ratios stated in claims 1-2 and 56 [sic] of the '808 Patent.

(JA16). The court made no "assumption" requiring support from an expert witness or otherwise, as CreAgri claims. Instead, the court relied on Romani, which specifically indicates that "[t]he aim of the present investigation was to evaluate

the polyphenolic content in different olive cultivars." (JA981). The entire point of Romani is to purify the phenols in order to quantify them as they naturally occur in different olive cultivars. The court merely expressed the obvious conclusion drawn from Romani's stated aim—that the methods would not alter the polyphenolic content the research sought to analyze. Indeed, CreAgri offered no evidence challenging this conclusion during summary judgment or on appeal.

CreAgri next misrepresents its expert's testimony in asserting that he "specifically opined that the weight ratios obtained in Romani were not the same as what was in the intermediate 'aqueous solution' or 'aqueous phase' . . . ." (CA36). But German observed only that "the weight ratios were not applied directly to an 'aqueous extract of olives' but to a heavily processed and purified solid composition akin to a dietary supplement." (JA1003). He offered no opinion whatsoever relating to any alteration of phenolic content based on a change of phase or purification. German's opinion must be further discounted in light of his misinterpretation of Romani as testing a solid extract, when in fact phenolic measurement was made on an extract dissolved in water. (JA984). The issue of fact CreAgri seeks to create based on German's opinion fails.

Romani's express disclosure of an "aqueous solution" derived from olives, coupled with its measurement of water-soluble phenols of material in the aqueous

phase, plainly satisfies the "aqueous extract of olives" limitation required by claims 1-2 and 5-6 of the '808 Patent, and anticipates those claims.

III. The District Court Correctly Found the '599 Patent Invalid Under the Written Description Requirement of 35 U.S.C. § 112.

Under 35 U.S.C. § 112(a), a patent specification must "contain a written description of the invention." 35 U.S.C. § 112. The written description "must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed." *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc) (internal quotations omitted).

The court correctly declared the '599 Patent invalid under the written description requirement because the specification does not support the treatment of the claimed inflammatory conditions using the claimed method and does not adequately describe the claimed dosage range. CreAgri, however, asserts that the '599 Patent meets the written description requirement because the specification provided enough "detailed information for one of skill in the art to understand what was being claimed" and because "prior art and prior knowledge of one of skill in the art supported written description of the '599 Patent." (CA38,CA42). Each of these arguments fail.

A. The '599 Patent Fails To Support Treatment of Inflammation Using the Claimed Method and Does Not Adequately Describe the Claimed Dosage Range.

The '599 Patent specification does not support the use of any hydroxytyrosol-rich composition to treat the inflammatory conditions claimed because the specification provides no data whatsoever to support the anti-inflammatory effects of the claimed olive-derived preparations. As the district court found, "the specification conclusively reveals that the inventor sought to claim a method of treating inflammation based on no more than a hope that olive-derived compositions would one day be used effectively to treat inflammation caused by a wide variety of factors." (JA20). "[V]ery little of the '599 Patent's specification is directed to treating inflammation using olive-derived phenols at all. Only about two-and-a-half columns of the nineteen-column specification discusses inflammation." (JA30). Instead of focusing on the claimed invention, the primary method discussed is one to treat an "AIDS-associated neurological disorder" (JA88-90(col.12,ln.30–col.14,ln.62.)) and "[a]ddional neurological diseases and disturbances contemplated for treatment by the method of the invention." (JA85(col.5,ln.31-32)). In addition, the '599 Patent discusses: HIV-1 Associated Dimentia (JA86(col.8,ln.1-63)), HIV-Associated Myelopathy (JA86(col.8,ln.64) – JA87(col.9,ln.12)), peripheral neuropathy (JA87(col.9,ln.13-46)), Cytomegalovirus (JA87(col.9,ln.47–col.10,ln.6)), Progressive Multifocal Leukoencephalopathy

(JA87(col.10,ln.7-21)), and methods of biological testing for AIDS-associated neurological disorders (JA88(col.11,ln.44–col.12,ln.29)). As the court further detailed, even under the inflammation subsection, the specification fails to explain why the inventor believed that olive-derived compositions were likely to treat any (much less all) of the claimed conditions.

The specification then provides four examples that are intended to "illustrate the invention." Each of these examples, however, is prospective and prophetic only. That is, the examples all described what Dr. Crea intended to do, but either had not yet started or had not yet completed at the time he filed the patent application. No evidence in the patent suggests that Dr. Crea performed this testing and obtained results demonstrating the utility of the claimed invention before the patent application was filed. Notably, not one of these examples describes any test establishing that hydroxytyrosol-rich compositions, as described in the claims, could be used to treat any of the claimed inflammatory conditions. (JA913-JA916).

Nor could they because, as Dr. Crea explained, the patent was "prophetic" because they "anticipate[d] that this would work" and "the patent was filed while [they] were doing the study, and the results weren't available." (JA909-JA911). "Requiring a written description of the invention limits patent protection to those who actually perform the difficult work of 'invention'—that is, conceive of the

complete and final invention with all its claimed limitations—and disclose the fruits of that effort to the public." *Ariad*, 598 F.3d at 1353. Accordingly, a prophetic approach to patenting is not proper, and a description, like here, that amounts "to no more than a 'wish' or 'plan' for obtaining the [claimed invention] does not satisfy the written description requirement." *Id.* at 1350 (internal citations omitted).

The '599 Patent represents nothing more than Dr. Crea's research plan at the time of filing the application. Even though Dr. Crea added the description of the examples in the '599 Patent through a nonprovisional application in February 2003, no results for those experiments were added to the patent. (JA912,JA913,JA916). The only suggestion of results performed prior to filing the patent application that led to the '599 Patent are "initial results" relating to isoprostane levels in urine. (JA91(col.18,ln.36-38)). This unreported data —even assuming it was in the possession of Dr. Crea at the time of filing—is inadequate because none of the patent claims relate to measurement of isoprostane in urine as a biochemical marker of oxidative stress. The patent does not describe any data regarding C-reactive protein, respiratory distress, or elevated CSF levels of isoprostanes, which are required by claim 1 for measurement of the anti-inflammatory effect. (JA913-916). Indeed, the specification indicates that CSF F2-

isoprostane assays would be performed separate from urinary tests. (JA91(col.17,ln.19-20)).

Moreover, there is no actual data reported and the sample size indicated is notably small. The specification itself states that the study is to be used only as "a pilot safety and tolerability study" and that "*statistical significance is not expected for the primary efficacy endpoint in this small study*." (JA91(col.18,ln.8-13)) (emph. added). This Court should refuse to "read the study's abbreviated findings as more persuasive than the patentee believed possible." (JA24). The specification similarly fails to provide any data relating to any change in inflammation caused by delayed type hypersensitivity reaction, psoriasis, an autoimmune disease, organ transplant, pain, fever, or tissue graft rejection, as required by claim 16. An adequate written description requires more than the mere possibility of anti-inflammatory effects that are only hypothesized in the specification.

CreAgri also asserts that the '599 Patent specification meets the written description requirement because "the inventor disclosed how to prepare compounds for use with the claimed methods of treatment." (CA38). But even if the specification "disclosed how to prepare compounds" this would not support the claimed invention because preparing compounds is wholly separate from actually using those compounds to treat the claimed conditions.

Next, CreAgri asserts that the specification meets the written description requirement because it includes "detailed examples of practicing the claimed methods." (CA38). But CreAgri fails to acknowledge that each of these four examples is prospective and prophetic only and therefore cannot support the claimed invention. (JA22-JA25).

As to Example 4, CreAgri asserts that the description is adequate because "it discusses *in vivo* studies implementing the claimed methods and monitoring markers or clinical symptoms such as the levels of C-reactive protein ('CRP') in the treatment of arthritis." (CA40). But as the district court detailed, "these proposed studies cannot describe the full scope of the claims, as arthritis is only relevant to two of the claimed seven ailments in claim 16 and none of the three in claim 1. Moreover, these study designs fail to disclose any results whatsoever, whether realized or predicted." (JA24).

The cases CreAgri relies on to assert that Example 4 meets the written description requirement without data are inapposite. (CA40). In *Falko-Gunter Falkner v. Inglis*, this Court confirmed that there may be limited circumstances where reduction to practice is not required, but "the applicant must convey to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention." 448 F.3d 1357, 1365 (Fed. Cir. 2006). There, the Court found that in light of the extensive disclosures in the specification and the state of the prior art at

the time, the invention was complete even though it had not been reduced to practice. This case is inapposite as there is no debate regarding reduction to practice. Rather, the Court here is determining whether the specification sufficiently supports the claimed invention, which it does not.

Union Oil Co. v. Atlanta Richfield, Co., 20 F.3d 989 (Fed. Cir. 2000), also does not support CreAgri's assertion that it need not show actual or anticipated results in the specification. The patent at issue there thoroughly discussed the complicated claimed ranges and combinations of multiple properties regarding gasoline products. But here, Dr. Crea was not in possession of the invention, there is no data whatsoever to indicate the invention was complete, there are no results from any studies to support the claims, and the state of the prior art did not support the specification.

Lastly, CreAgri asserts that the district court erroneously dismissed parts of the '599 Patent specification as irrelevant because it discussed treatment of a "neurological disorder" associated with AIDS. (CA41). CreAgri mischaracterizes and oversimplifies the district court's findings. Indeed, in support of this argument, CreAgri continues to cite to portions of the specification that have nothing to do with the claimed conditions, such as whether CMV may be cultured from the CSF, and statements regarding bronchial asthma, rheumatoid arthritis, and general inflammation giving rise to oxidative stress. (CA42). The district court

properly reviewed the '599 Patent specification and found that there was no data whatsoever to support the claimed conditions, including in the portion of the specification discussing a neurological disorder associated with AIDS.

B. The District Court Applied the Correct Standard Under § 112.

CreAgri takes issue with the district court's "overly stringent standard for written description by requiring actual medical proof of the claimed inventions within the specification rather than just disclosure sufficient to one of skill in the art." (CA37). As an initial matter, the court adopted CreAgri's proposed lower level of skill for one of ordinary skill in the art, but ultimately found that because the specification provides no data whatsoever, the level of ordinary skill in the art is irrelevant. (JA20,fn.12).

The district court did not rewrite the claims of the '599 Patent as CreAgri asserts. The '599 Patent focuses on methods of using phenolic compounds to treat specific inflammatory conditions. CreAgri suggests that there is some level of "effectiveness" for treatment of inflammatory conditions that does not rise to the level of "medical effectiveness." Essentially, CreAgri is arguing that the specification sufficiently describes a medically ineffective treatment. This argument is nonsensical. The Court's one-time mention of "medical efficacy" in over ten pages of its opinion relating to written description does not render its detailed analysis erroneous.

C. The State of the Art at the Time the '599 Patent Was Filed Does Not Support the Written Description Requirement.

Despite CreAgri's assertion otherwise, "[t]ypically, patent applications claiming new methods of treatment are supported by test results." *In re '318 Patent Infringement Litig.*, 583 F.3d 1317, 1324 (Fed. Cir. 2009). In *'318 Patent Infringement*, this Court found that "neither in vitro test results nor animal test results involving the use of galantamine to treat Alzheimer's-like conditions were provided. The results from the '318 patent's proposed animal tests of galantamine for treating symptoms of Alzheimer's disease were not available at the time of the application, and the district court properly held that they could not be used to establish enablement." *Id.* at 1325. Like here, "the specification, even read in the light of the knowledge of those skilled in the art, does no more than state a hypothesis and propose testing to determine the accuracy of that hypothesis. That is not sufficient." *Id.* at 1327.

The absence of data in the '599 Patent showing anti-inflammatory activity of the claimed treatment agents is particularly significant in light of the state of the art in the 2002 time period. At the time the application leading to the '599 Patent was filed, researchers had published studies showing the effects of olive phenols on biochemical markers and enzymes thought to be involved in inflammation. For example, Dr. Visioli had researched LTB_4, which suggested that hydroxytyrosol found in olive wastewater had anti-inflammatory potential. (JA945-49). Others in

the field also suggested that enzymes involved in inflammatory processes could be inhibited by olive phenols. (JA1048-63). Other publications suggesting the anti-inflammatory potential of olive phenols are detailed above.

But, as detailed in the expert report of Dr. Visioli, none of these prior art publications describe an *in vivo* effect of olive phenols on any of the specific biochemical markers or symptoms claimed in the '599 Patent. (JA1086-87). Nor do any of these publications describe hydroxytyrosol as conferring *in vivo* anti-inflammatory activity in humans or any animal, for that matter. (*Id.*).

The publications CreAgri relies on suggest that administration of hydroxytyrosol or oleuropein *might* reduce inflammation, but there is no indication that administration of a hydroxytyrosol-rich composition (or a substantially purified hydroxytyrosol composition) would in fact alter the biochemical markers for or clinical symptoms of any of the inflammatory conditions listed in claims 1 and 16 of the '599 Patent:

- **Fehri**: CreAgri relies on Fehri because it discusses a dried leaf extract "containing 3.2% of oleuropein" showing an anti-inflammatory effect on carrageenan induced oedema. (CA43). But CreAgri cannot cite to anything in Fehri related to a hydroxytyrosol-rich composition or any of the conditions claimed in the '599 Patent. Fehri only suggests that anti-inflammatory effects "could be investigated in therapeutics." (JA2709).

- **Ragione**: Ragione relates to tests of hydroxytyrosol for apoptogenic activity, including in two colon cell lines that "were completely resistant to the apoptogenic capability of DPE." (JA27). CreAgri asserts that the court had no evidence to determine that one of skill in the art would find "the aberrant cell lines to affect the reasonable expectation that the hydroxytyrosol had anti-inflammatory benefits." (CA44). But even if this were true, CreAgri points to nothing in Ragione relating to the clinical symptoms of any of the inflammatory conditions listed in claims 1 and 16.
- **Visioli**: CreAgri relies on Visioli because it "suggest[s] that OMWW extracts exert biological effects beyond their antioxidant properties." (CA45). But like the '599 Patent specification, Visioli is merely prophetic and it even confirms that "[a]dditional studies are needed."
- **Kohyama and Petroni**: CreAgri makes a conclusory statement that these references "also showed that the administration of hydroxytyrosol has [*sic*] the potential to reduce inflammation." (CA45). CreAgri cites to nothing specific in these articles to support its contention that this prior art supports the specification of the '599 Patent. As the district court found, these articles at most are prophetic regarding anti-inflammatory use of hydroxytyrosol because both stress the need for *in vivo* testing.

Accordingly, in light of the lack of data and the status of the prior art at the time the patent was filed, there is no indication that one skilled in the art would accept without question the statements in the '599 Patent as to the effects of the claimed drug products.

"Requiring a written description of the invention limits patent protection to those who actually perform the difficult work of invention—that is, conceive of and complete the final invention. The written description requirement exists to ensure that inventors do not attempt to preempt the future before it has arrived." *Billups-Rothenberg, Inc. v. Ass'd Regional & Univ. Pathologists, Inc.*, 642 F.3d 1031, 1036 (Fed. Cir. 2011). The lack of data in the '599 Patent specification shows that Dr. Crea did not actually invent the invention claimed. "[A] mere wish or plan for obtaining the claimed invention is not adequate." *Centocor Ortho Biotech, Inc. v. Abbott Labs.*, 636 F.3d 1341, 1348 (Fed. Cir. 2006). As the district court found, "neither the claims nor the specification discloses that the inventor possessed a treatment for inflammation caused by any of the claimed conditions, much less all of them." (JA22). The specification of the '599 Patent thus fails to adequately describe the claimed method of treating inflammatory conditions.

D. There Is No Evidence that the District Court Had Any Preconceived View of Written Description That Improperly Colored Its Analysis.

CreAgri suggests that the court had a faulty premise regarding the written description requirements for patents in the field of chemical arts. (CA47). But CreAgri's attempt to avoid the district court's detailed analysis on this basis is confounding. The district court's careful analysis of the '599 Patent is supported by both the law and evidence.

In setting forth the law for written description, the court cited to cases related to claims that have a chemical nature to show that chemical arts are unpredictable. The court only cited to *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916 (Fed. Cir. 2004), as an example of a case where a patent directed toward treatment of inflammation was found to lack a sufficient written description. (JA19). In that case, the Court found that the patent-at-issue failed the written description requirement because no language in the specification described compounds that achieve the claimed effect. "It [was] clear from reading the patent that one critical aspect of the method—a compound that selectively inhibits PGHS-2 activity—was hypothetical, for it is clear that the inventors had neither possession nor knowledge of such a compound." *Id.* at 926. Similarly, the '599 Patent specification lacks critical aspects of the invention; namely, any data to

support the use of any hydroxytyrosol-rich composition to treat the inflammation conditions claimed.

IV. The District Court Correctly Found the '599 Patent Invalid Under the Enablement Requirement of 35 U.S.C. § 112.

The written description and enablement requirements under the first paragraph of 35 U.S.C. § 112, "while related and springing from the same factual predicates, each have a separate purpose." *Crown Operations Intern., Ltd. v. Solutia Inc.*, 289 F.3d 1367, 1378-79 (Fed. Cir. 2002). "The purpose of the written description requirement is to ensure adequate disclosure of the invention." *Pozen, Inc. v. Par Pharm., Inc.*, 696 F.3d 1151, 1166 (Fed. Cir. 2012) (internal citations omitted). The purpose of the enablement requirement, however, is to "ensure[ ] that the public knowledge is enriched by the patent specification to a degree at least commensurate with the scope of the claims." *Crown Operations Intern, Ltd.*, 289 F.3d at 1378 (internal quotations omitted).

To satisfy the enablement requirement of 35 U.S.C. § 112, ¶ 1, the patent specification must "describe the claimed invention so that one skilled in the art can recognize what is claimed." *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 968 (Fed. Cir. 2002). In other words, the patent's "disclosure must allow one skilled in the art 'to visualize or recognize the identity of' the subject matter purportedly described." *Id.* (internal quotations omitted); *see also Cordis Corp. v. Medtronic Ave, Inc.*, 339 F.3d 1352, 1364 (Fed. Cir. 2003).

In an enablement analysis, the Court must first determine whether the claims are supported by the specification. *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1371-74 (Fed. Cir. 1999). The second determination is whether a person skilled in the art can make and use the invention without undue experimentation. *Id.*

All of the asserted claims of the '599 Patent relate to treatment of inflammation with either (1) hydroxytyrosol and oleuropein in a specific weight ratio or (2) substantially purified hydroxytyrosol or mixture of hydroxytyrosol and oleuropein. The '599 Patent does not enable treatment of inflammation using the claimed methods. "[T]he how to use prong of section 112 incorporates as a matter of law the requirement of 35 U.S.C. § 101 that the specification disclose as a matter of fact a practical utility for the invention. … [A]n applicant's failure to disclose how to use an invention may support a rejection under either section 112, paragraph 1 for lack of enablement, or section 101 for lack of utility when there is a complete absence of data supporting the statements which set forth the desired results of the claimed invention." *Rasmussen v. Smithkline Beecham Corp.*, 413 F.3d 1318, 1323 (Fed. Cir. 2005). "[W]here there is no indication that one skilled in [the] art would accept without question statements [as to the effects of the claimed drug products] and no evidence has been presented to demonstrate that the

claimed products do have those effects, an applicant has failed to demonstrate sufficient utility and therefore cannot establish enablement." *Id.*

As with the written description argument, CreAgri again asserts that the court used an improperly heightened standard for enablement because it required "one to prove medical efficacy of the claimed methods of treatment and disclose FDA clinical trials." (CA48). As set forth above, CreAgri's assertion that the treatment could be something other than "medically efficient" is nonsensical. In addition, CreAgri mischaracterizes the court's opinion because it did not find that CreAgri would have had to disclose results from an FDA clinical trial. In fact, the district court recognized that "testing need not be conducted by the inventor, and human trials are not required." (JA29). Instead, the court found that CreAgri had not disclosed results from *any* relevant trial or even *in vitro*. CreAgri has still not identified any data to support the use of a compound within the claimed ratios for hydroxytyrosol and oleuropein that are effective in treating the claimed conditions (rather than just any inflammation, as CreAgri continuously asserts is sufficient).

An inventor may rely on *in vitro* studies to support a claimed invention only if the studies have actual results that support the claimed method. *In re '318 Patent Infringement Litig.*, *supra*, 583 F.3d at 1324. Like here, the Court in *'318 Patent Infringement Litigation* found that "the ['318 Patent] specification, even read in the light of the knowledge of those skilled in the art, does no more than

state a hypothesis and propose testing to determine the accuracy of that hypothesis. That is not sufficient." *Id.* at 1327. In *Brana,* this Court held that the patent applicants had established the utility of claimed therapeutic compounds by presenting in vitro test results and evidence of structural similarity between the claimed and prior art compounds when filing the patent application. *In re Brana*, 51 F.3d 1560, 1566 (Fed. Cir. 1995). The evidence presented to demonstrate in vivo effectiveness was that the "specification illustrates the cytotoxicity of the claimed compounds against human tumor cells, *in vitro.*" *Id.* at 1563. Thus, *Brana* relied upon evidence of efficacy in a disease model to demonstrate enablement. *Id.* Here, however, CreAgri has not identified any model for the claimed inflammatory conditions, nor does the specification contain any evidence of efficacy in any disease model whatsoever.

The district court correctly found that the prospective examples in the '599 Patent specification fail to enable the claimed invention.

> If mere plausibility were the test for enablement under section 112, applicants could obtain patent rights to inventions consisting of little more than respectable guesses as to the likelihood of their success. When one of the guesses later proved true, the inventor would be rewarded the spoils instead of the party who demonstrated that the method actually worked. That scenario is not consistent with the statutory requirement that the inventor enable an invention rather than merely proposing an unproved hypothesis.

In re '318 Patent Infringement Litig., 583 F.3d at 1327.

A. The Court Did Not Improperly Shift the Burden To CreAgri .

CreAgri contends that the district court erred by improperly shifting the burden to CreAgri because Pinnaclife failed to show that undue experimentation would be required to practice the claimed methods of the '599 Patent. As detailed herein, the '599 Patent specification provides no data whatsoever supporting the claimed method for treating the claimed conditions. The examples provided in the specification merely suggest studies that may be done, but that have not actually been completed and have not yet yielded any results. The fact that one of ordinary skill in the art would have to be the first person to actually complete an experiment supporting the claimed method is certainly undue experimentation.

CreAgri relies on *Cephalon v. Watson Pharmaceuticals, Inc.*, 707 F.3d 1339 (Fed. Cir. 2013), to assert that Pinnaclife did not meet its burden because "unsubstantiated statements indicating that experimentation would be difficult and complicated are not sufficient." (CA51). But *Cephalon* actually supports the district court's findings here. In *Cephalon*, this Court rejected the lower court's analysis, which was based on expert testimony that was "largely unsupported" and therefore "carrie[d] little weight" because the expert merely opined that certain experimentation would be "very difficult" and "complicated." *Id.* at 1338. The Court found that "the focus is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in

question provides a reasonable amount of guidance." *Id.* at 1339 (internal quotations omitted). The Court found that the patents-at-issue were not invalid for lack of enablement because the movant "ha[d] not presented evidence showing why formulations for a [effervescent] 'couple' do not provide sufficient guidance for a skilled artisan to calculate formulations for single compound effervescent agents." *Id.*

The '599 Patent specification does not provide guidance for any of the claimed methods. This Court has "held that the amount of experimentation would be undue where: (1) the specification lacks guidance by teaching away from the subject matter that was eventually claimed; and (2) there is evidence of the patentee's own failures to make and use the later claimed invention at the time of the application." *Id., citing AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003). And, "when a range is claimed, there must be reasonable enablement of the scope of the range." *AK Steel Corp.*, 344 F.3d at 1244. As detailed above, here, "the specification's teaching is itself evidence that at least a significant amount of experimentation would have been necessary to practice the claimed invention." *Id.*

B. CreAgri's Expert Failed To Create an Issue of Fact.

The district court considered CreAgri's expert's testimony that one of skill in the art would have read the disclosure in the '599 Patent and understood how to

use the claimed methods, but properly rejected it because it failed to create an issue of fact. As the court noted, German failed to contradict Visioli's report that "[b]y 2002, no researcher working in the field of olive-derived polyphenols had published reliable data establishing that either hydroxytyrosol or oleuropein showed *in vivo* anti-inflammatory activity." (JA1077). Or that "in the 1999-2002 time period, anti-inflammatory activity could not be inferred from research showing that olive-derived polyphenols exhibit antioxidant activity." (JA1077).

There was no "disagreement between experts," as CreAgri contends. (CA54). Instead, German simply claimed that he was "unable to determine the evidentiary basis" of Visioli's opinions and he cited two articles written by Visioli that he contends "assert that antioxidant activity was related to anti-inflammatory activity in 2001 and 2002." (JA998). But German did not reject or otherwise controvert either of Visioli's opinions that the therapeutic effect of olive-derived polyphenols had not been established in the art.

When CreAgri failed to provide a copy of Visioli's articles to the court, "[t]o avoid any doubt, the Court independently obtained and examined the two articles authored by Dr. Visioli and cited by Dr. German, and [] discovered that neither establishes a recognition in the art of the therapeutic effects of olive-derived polyphenols." (JA31). CreAgri has not asserted any facts contrary to the court's findings as both articles only disclose a hope that phenolic compounds in olives

could have therapeutic effects. Indeed, both articles run contrary to CreAgri's position as they specifically conclude that "[i]n the future, the availability of pure, or even labeled, compounds in adequate quantities and the development of appropriate methodologies will clarify the metabolic fate of phenolic micronutrients, including those of olive oil." (JA3330,JA3338).

V. The District Court Correctly Found the '599 Patent Invalid Because It Lacks Utility Under 35 U.S.C. § 101.

In addition to claiming an invention within one of the subject matter categories provided in Section 101, a patent must also show that the claimed invention is "useful." 35 U.S.C. § 101. Often times where a patent lacks utility under Section 101, it also is deficient under Section 112—i.e., if an invention lacks utility, an application for that invention cannot enable one to use it. *See In re Ziegler*, 992 F.2d 1197, 1200-01 (Fed. Cir. 1993). To demonstrate that an invention is useful, an applicant must show that (1) a person of ordinary skill in the art would immediately appreciate why the invention is useful based on the characteristics of the invention, and (2) the utility is specific, substantial, and credible. *In re Fisher,* 421 F.3d 1365, 1370-72 (Fed. Cir. 2005). Thus, "[i]f a patent claim fails to meet the utility requirement because it is not useful or operative, then it also fails to meet the how-to-use aspect of the [section 112] enablement requirement." *In re '318 Patent Infringement Litig.*, *supra*, 583 F.3d at 1324.

As the district court found, because "[e]nablement, or utility, is determined as of the application filing date," *In re Brana*, 51 F.3d 1560, 1567n.19 (Fed. Cir. 1995), an invention will not be considered useful for the purposes of section 101 where, at the time of filing, "there is a complete absence of data supporting the statement which set forth the desired results of the claimed invention"—even if the invention is later proven useful or operable. *Rasmusson,* 413 F. 3d at 1323 (quotations omitted); *see also Brenner v. Manson,* 383 U.S. 519, 535 (1966) ("Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing."). Furthermore, "[i]f mere plausibility were the test for [enabling disclosures of utility] under section 112, applicants could obtain patent rights to 'inventions' consisting of little more than respectable guesses as to the likelihood of their success." *Rasmusson,* 413 F.3d at 1325. But the Patent Act does not provide for the patenting of mere research proposals or hypotheses. *In re '318 Patent Infringement Litig.*, 583 F.3d at 1324. "[A] patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." *Brenner*, 383 U.S. at 536.

Here, the '599 Patent lacks utility. When Dr. Crea was asked about the treatment agent of claim 1, he admitted there are no results described in the '599 Patent that show that the treatment agent has an effect on levels of C-reactive protein, respiratory distress in the case of bronchial inflammation, or on clinical

symptoms determined from neuropsychological testing in the case of neuroinflammation. (JA913-JA916). Since nothing in the patent specification supports the effects detailed in claim 1, the patent fails to show that the purported invention is useful as disclosed in its current form. As discussed above, the experiments detailed in the '599 Patent were all prospective. To establish substantial utility, however, an applicant must show that an invention is useful as disclosed in its current form, rather than at some time in the future pending additional research. *In re Fisher*, 421 F.3d at 1371.

CreAgri asserts that the district court erred in dismissing "at least two peer-reviewed articles published after the filing date of the '599 Patent" that were authored by the inventor of the '599 Patent. (CA56). But CreAgri does not appeal the Court's finding that "the Court cannot consider CreAgri's post-filing test results as evidence of the utility of the claimed methods of treating inflammation. Enablement is determined as of the effective filing date of the patent's application. Where results were not available at the time of the application, they cannot be used to establish utility or enablement." (JA33). Accordingly, the district court's findings should be affirmed. *See Greenwood*, *supra*, 28 F. 3d at 977.

Even if this Court could consider CreAgri's argument regarding the import of the post-filing articles, it does not create an issue of fact as to whether persons of ordinary skill in the art would accept the utility of the claimed treatment as of the

filing date of the invention. CreAgri completely ignores the district court's finding that the first article, "Hydrolyzed Olive Vegetation Water in Mice Has Anti-Inflammatory Activity," demonstrates that the effectiveness of hydroxytyrosol as an anti-inflammatory was still uncertain because it concluded that "although the major phenolic compound of hydrolyzed olive water is [hydroxytyrosol], the anti-inflammatory activity [found in the study] may be attributable to another component of the water that is as yet unidentified." (JA2753).

The second article, "Olive extract supplement decreases pain and improves daily activities in adults with osteoarthritis and decreases plasma homocysteine in those with rheumatoid arthritis," is equally unhelpful to CreAgri's position. As the district court found, "the arthritis study cannot enable any of the '599 Patent's claims, as it does not mention hydroxytyrosol or oleuropein," and, in any event, it "cannot enable the full scope of the '599 Patent's claims because it only deals with the treatment of arthritis, without mention any of the other claimed ailments." (JA34). Significantly, although the study mentions "OVW," it does not relate to specific ratios of hydroxytyrosol and oleuropein as it relates to the treatment of the claimed conditions. (JA2750). CreAgri's position that the '599 Patent is enabled by studies related to olive vegetation water's anti-inflammatory effect for any condition—not just the claimed conditions—is unsupported by any law or evidence.

CreAgri also fails to distinguish the authority the district court relied on to find that the '599 Patent lacks utility. In *'318 Patent Infringement Litigation*, this Court noted that circumstances where analytic reasoning alone will demonstrate utility are likely to be rare. 583 F.3d at 1326. As the district court detailed, there, this Court upheld a ruling of invalidity concerning a patent for a method of treating Alzheimer's disease where the specification grounded the compound's efficacy on its other known effects as described in scientific literature and made no reference to either *in vitro* or *in vivo* testing. *Id.* at 1326. While the Court did not rule out the possibility of disclosing utility through "analytic reasoning" based on known properties, it found that any analytic insights made by the inventor were "nowhere described in the specification," and therefore did not reach the question of whether such insights were sufficient. *Id.* CreAgri continues to assert that the '599 Patent, confirmed in its post-filing publications, showed the practical utility of the claimed inventions. But as set forth above, nothing in the '599 Patent specification supports the claimed invention and the specification does not explicitly provide any analytic reasoning as to why the invention would work as claimed.

As to the court's reliance on *Brana* and *Actavis*, CreAgri confuses the district court's holding. The district court did not rely on those cases to assert that CreAgri must conduct FDA testing in order to prove utility. Rather, the court distinguished those cases because, unlike here, each involved patents that detailed

results relevant to the claimed invention. In *Brana*, the patentee disclosed certain *in vitro* results of the claimed compound's effectiveness and the claimed compound was structurally similar to a compound proven to be effective *in vivo*. 51 F.3d at 1563, 1567. In *Actavis*, the Court considered that the FDA authorized a human clinical trial for the claimed treatment because this shows that the applicant had provided a convincing rationale to those especially skilled in the art (i.e., the FDA) that the investigation may be successful. *Eli Lily & Co. v. Actavis Elizabeth, LLC*, 435 F.Appx. 917, 924 (Fed. Cir. 2011). CreAgri cannot rely on these cases because the '599 Patent specification discloses no results regarding the claimed therapy. Rather, the '599 Patent claims a research hypothesis, which "do[es] not qualify for patent protection." *Ariad*, 598 F.3d at 1353. The court did not err in holding the '599 Patent invalid for lack of utility.

CONCLUSION

Based on the foregoing, the judgment of invalidity of the '808 and '599 Patents should be affirmed in its entirety.

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Respectfully submitted,

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PROOF OF SERVICE

I hereby certify that on 22nd day of May, 2014, the foregoing Brief of Defendant-Appellee Pinnaclife, Inc. was filed electronically with the court, to be served upon all counsel of record by utilization of the Court's electronic filing system and email upon the following. I further certify that the original and five copies were sent to the Clerk, United States Court of Appeals for the Federal Circuit, and that two copies of the foregoing document were served upon counsel listed below by ECF:

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CERTIFICATE OF COMPLIANCE

This Brief for Defendant-Appellee Pinnaclife, Inc. complies with the type-volume limitation of Federal Rule of Appellate Procedure ("FRAP") 32(a)(7)(B) as it contains 13,827 words, excluding the parts of the brief exempted by FRAP 32(a)(7)(B)(iii).

This Brief complies with the typeface requirements of FRAP 32(a)(5) and the type style requirements of FRAP 32(a)(6) because the brief has been prepared in a proportionally spaced typeface using Times New Roman in 14-point regular type.

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